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=> b reg;d que sta 18
FILE 'REGISTRY' ENTERED AT 09:02:44 ON 01 MAY 2007
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provided by InfoChem.

STRUCTURE FILE UPDATES:   30 APR 2007  HIGHEST RN 933825-30-0
DICTIONARY FILE UPDATES:  30 APR 2007  HIGHEST RN 933825-30-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

L6              STR
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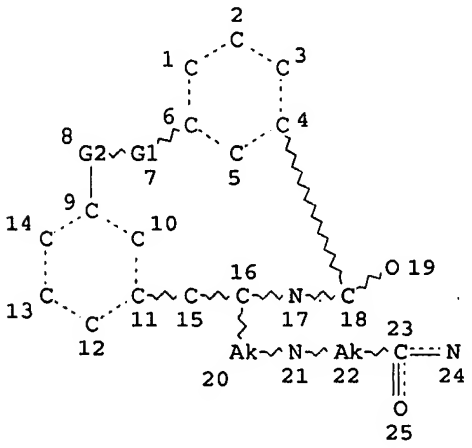


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REP G2=(3-3) CH2
NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L8            34 SEA FILE=REGISTRY SSS FUL L6

100.0% PROCESSED   63422 ITERATIONS                      34 ANSWERS
SEARCH TIME: 00.00.03


=> b hcap;d bib abs fhitstr hitrn retable l10 tot
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FILE 'HCAPLUS' ENTERED AT 09:03:12 ON 01 MAY 2007

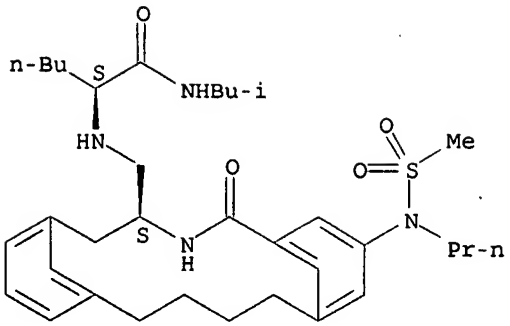
FILE COVERS 1907 - 1 May 2007 VOL 146 ISS 19
FILE LAST UPDATED: 30 Apr 2007 (20070430/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L10 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1149497 HCAPLUS
DN 146:19371
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model. [Erratum to document cited in CA145:465146]
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Wu, Guoxin; Crouthamel, Michelle; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(24), 7252
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Guoxin Wu and Michelle Crouthamel were inadvertently omitted from the author list. Their affiliation is the Department of Biol. Chemical, represented by the double dagger symbol in the paper. The correct author list is given.
IT **847157-19-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

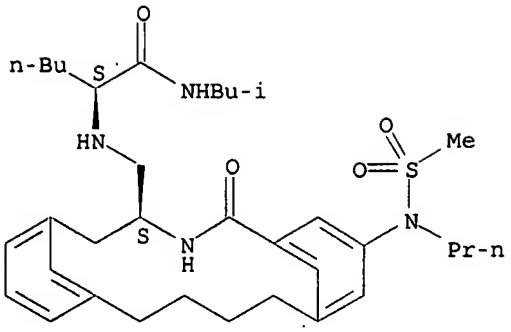
Absolute stereochemistry.



IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model (Erratum))

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:908572 HCAPLUS
DN 145:465146
TI Macrocyclic Inhibitors of β-Secretase: Functional Activity in an Animal Model
AU Stachel, Shawn J.; Coburn, Craig A.; Sankaranarayanan, Sethu; Price, Eric A.; Pietrak, Beth L.; Huang, Qian; Lineberger, Janet; Espeseth, Amy S.; Jin, Lixia; Ellis, Joan; Holloway, M. Katharine; Munshi, Sanjeev; Allison, Timothy; Hazuda, Daria; Simon, Adam J.; Graham, Samuel L.; Vacca, Joseph P.
CS Department of Medicinal Chemistry, Biological Chemistry, Molecular Systems and Structural Biology, Merck Research Laboratories, West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (2006), 49(21), 6147-6150
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A macrocyclic inhibitor of β-secretase was designed by covalently crosslinking the P1 and P3 side chains of an isophthalamide-based inhibitor. Macrocyclization resulted in significantly improved potency and phys. properties when compared to the initial lead structures. More importantly, these macrocyclic inhibitors also displayed in vivo amyloid lowering when dosed in a murine model.
IT **847157-19-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)
RN 847157-19-1 HCAPLUS
CN Hexanamide, N-(2-methylpropyl)-2-[[[(4S)-17-[(methylsulfonyl)propylamino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT **847157-19-1P 847157-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrocyclic inhibitors of β-secretase and functional activity in an animal model)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Beher, D	2005	14	1385	Expert Opin Invest D	HCAPLUS
Best, B	2005	313	902	Pharmacol Exp Ther	
Brady, S	2004	14	601	Bioorg Med Chem Lett	HCAPLUS
Cai, H	2001	4	233	Nat Neurosci	HCAPLUS
Coburn, C	2006	16	3635	Bioorg Med Chem Lett	HCAPLUS
Goate, A	1991	349	523	Nature	
Hannessian, S	2006	49	4544	J Med Chem	
Hardy, J	1997	349	704	Proc Natl Acad Sci U	
Hu, X	2004	47	4941	J Med Chem	HCAPLUS
Lamb, B	1993	5	22	Nat Genet	HCAPLUS
Lamb, B	1993	5	22	Nature Genetics	HCAPLUS
Milano, J	2004	82	341	Toxicol Sci	HCAPLUS
Roberds, S	2001	10	1317	Hum Mol Genet	HCAPLUS
Rojo, I	2006	16	191	Bioorg Med Chem Lett	HCAPLUS
Sankaranarayanan, S	2006			10th International c	
Savage, M	1998	18	1743	J Neurosci	HCAPLUS
Scholl, M	1999	1	953	Org Lett	HCAPLUS
Searfoss, G	2003	278	46107	J Biol Chem	HCAPLUS
Selkoe, D	1996	271	18295	J Biol Chem	HCAPLUS
Selkoe, D	1999	399A	23	Nature	
Simon, A	2005			2005 AD/PD meeting	
Sinha, S	1999	96	11049	Proc Natl Acad Sci U	HCAPLUS
Stachel, S	2006	16	641	Bioorg Med Chem Lett	HCAPLUS
Stachel, S	2004	47	6117	J Med Chem	
Stachel, S	2004	47	6447	J Med Chem	HCAPLUS
Thompson, L	2005	11	3383	Curr Pharm Des	HCAPLUS
Tilley, J	1991	34	1125	J Med Chem	HCAPLUS
Tsantrizos, Y	2003	42	1356	Angew Chem, Int Ed	HCAPLUS

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:177829 HCAPLUS
DN 142:280070
TI Preparation of macrocyclic β-secretase inhibitors for the treatment of Alzheimer's disease
IN Coburn, Craig; Stachel, Shawn J.; Vacca, Joseph P.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2005018545	A2	20050303	2004WO-US25791	20040810
	WO2005018545	A3	20050519		
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	AU2004266605	A1	20050303	2004AU-0266605	20040810
	CA---2535337	A1	20050303	2004CA-2535337	20040810
	EP---1656359	A2	20060517	2004EP-0780598	20040810
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	CN---1835936	A	20060920	CN 2004-80023327	20040810
	JP2007502278	T	20070208	2006JP-0523290	20040810
	US2007037784	A1	20070215	2006US-0568153	20060213
PRAI	2003US-495667P	P	20030814		
	2004WO-US25791	W	20040810		

OS CASREACT 142:280070; MARPAT 142:280070

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Macrocyclic compds. of formula I [R1 = H, R4-S(O)pN(R5), CN, etc.; R2, R3 = H, alkyl, halo, OH, alkoxy, etc.; R4 = alkyl, (substituted) NH2, Ph, benzyl, etc.; R5 = H, alkyl, Ph, benzyl; p = 0-2; X = CH2, O] are prepared which are inhibitors of the β-secretase enzyme and that are useful in the treatment or prevention of diseases such as Alzheimer's disease. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the β-secretase enzyme is involved. Thus, II was prepared from Me 3-nitrobenzoate, allyltributyl stannane, m-allyltyrosine Me ester hydrochloride and N-isobutyl-L-norleucineamide hydrochloride in several steps. The compds. had IC50 from about 1 nM to 1 μM against β-secretase enzyme.

IT **847157-12-4P**

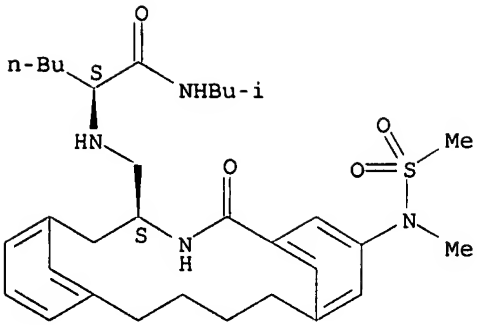
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

RN 847157-12-4 HCAPLUS

CN Hexanamide, 2-[[[(4S)-17-[methyl(methylsulfonyl)amino]-2-oxo-3-azatricyclo[13.3.1.16,10]eicosa-1(19),6,8,10(20),15,17-hexaen-4-yl]methyl]amino]-N-(2-methylpropyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **847157-12-4P 847157-13-5P 847157-14-6P**
847157-15-7P 847157-16-8P 847157-17-9P
847157-18-0P 847157-19-1P 847157-20-4P
847157-21-5P 847157-22-6P 847157-23-7P
847157-24-8P 847157-25-9P 847157-26-0P
847157-28-2P 847157-30-6P 847157-31-7P
847157-32-8P 847157-33-9P 847157-34-0P
847157-35-1P 847157-36-2P 847157-37-3P
847157-38-4P 847157-39-5P 847157-40-8P
847157-41-9P 847157-42-0P 847157-43-1P
847157-44-2P 847157-45-3P 847157-46-4P
847225-40-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of macrocyclic β-secretase inhibitors for treatment of Alzheimer's disease)

=> b wpix
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FILE LAST UPDATED: 26 APR 2007 <20070426/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200727 <200727/DW>
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>>> New reloaded DWPI Learn File (LWPI) available as well <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> New display format FRAGHITSTR available <<<
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http://www.stn-international.de/archive/stn_online_news/fraghitstr_ex.pdf

>>> IPC Reform backfile reclassification has been loaded to 31 December 2006. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC. <<<

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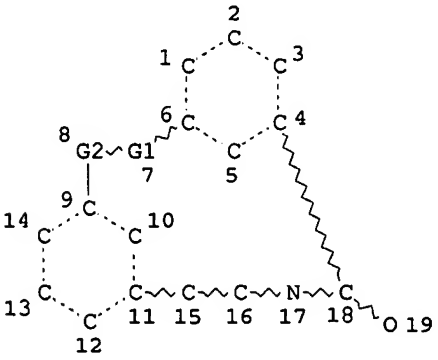
FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
'BI BIEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que sta l17
L1 STR



VAR G1=O/CH2
REP G2=(3-3) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L17 32 SEA FILE=WPIX SSS FUL L1

100.0% PROCESSED 9531 ITERATIONS 32 ANSWERS
SEARCH TIME: 00.00.07

=> d bib abs dcn l20 tot

L20 ANSWER 1 OF 1 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
AN 2005-202434 [21] WPIX
DNC C2005-064723 [21]
TI New 3-aza-tricyclo-icosa-hexaene derivatives useful as macrocyclic beta-secretase inhibitor for treating Alzheimer's disease
DC B02
IN COBURN C; STACHEL S; STACHEL S J; VACCA J; VACCA J P; COBURN C A
PA (MERI-C) MERCK & CO INC; (COBU-I) COBURN C A; (STAC-I) STACHEL S J; (VACC-I) VACCA J P
CYC 107
PIA WO--2005018545 A2 20050303 (200521)* EN 42[0]
EP-----1656359 A2 20060517 (200634) EN
AU--2004266605 A1 20050303 (200663) EN
CN-----1835936 A 20060920 (200706) ZH
JP--2007502278 W 20070208 (200713) JA 38
US-20070037784 A1 20070215 (200715) EN
ADT WO--2005018545 A2 2004WO-US0025791 20040810; AU--2004266605 A1 2004AU-000266605 20040810; CN-----1835936 A 2004CN-080023327 20040810; EP-----1656359 A2 2004EP-000780598 20040810; EP-----1656359 A2 2004WO-US0025791 20040810; JP--2007502278 W 2004WO-US0025791 20040810; JP--2007502278 W 2006JP-000523290 20040810; US-20070037784 A1 Provisional

2003US-000495667P 20030814; US-20070037784 A1 2004WO-US0025791 20040810; US-20070037784 A1 2006US-000568153 20060213

FDT EP-----1656359 A2 Based on WO--2005018545 A; AU--2004266605 A1 Based on WO--2005018545 A; JP--2007502278 W Based on WO--2005018545 A

PRAI 2003US-000495667P 20030814
2006US-000568153 20060213

AN 2005-202434 [21] WPIX

AB WO 2005018545 A2 UPAB: 20060121

NOVELTY - 3-Aza-tricyclo-icosa-hexaene derivatives are new.

DETAILED DESCRIPTION - 3-Aza-tricyclo-icosa-hexaene derivatives of formula (I) are new.

R1 = H, R4S(O)pN(R5), CN, 1-6C alkyl-CN, halo, phenyl (optionally mono- - penta-substituted with CN, halo, 1-6C alkyl, OR5, CO2R5 or C(O)R5 or group of formula (i);

R4 = 1-8C alkyl (optionally substituted 1 to 7 times by F), NR5R6, phenyl or benzyl;

R5 and R6 = H, 1-6C alkyl (optionally mono- - hexa-substituted with F), phenyl or benzyl;

p = 0 - 2;

R2 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl (all optionally substituted 1 to 7 times with halo, hydroxy, O-1-6C alkyl, 3-6C cycloalkyl, S(O)p-1-6C alkyl, CN, CO2H, CO2-1-6C alkyl, CO-NR5R6) or phenyl (optionally substituted 1 to 5 times with T), H or phenyl (optionally mono- - penta-substituted with T);

T = 1-6C alkyl, CN, halo, CF3, O-R5 or CO2R5);

R3 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl (all optionally substituted 1 to 7 times halo, hydroxy, trifluoromethyl, O-R5, CO2R5 , S(O)pN(R5)-1-6C alkyl, S(O)pN(R5)-phenyl, phenyl, pyridyl (both optionally substituted 1 to 5 times with T), phenyl (optionally mono- - penta-substituted by T);

X = CH2 or O.

ACTIVITY - Nootropic; Neuroprotective; Hemostatic; Cerebroprotective; Vulnerary; Vasotropic; Antiinflammatory; Antidiabetic; Antiarteriosclerotic.

MECHANISM OF ACTION - beta-Secretase activity inhibitor. The inhibitory activity of (I) is confirmed by HPLC assay. (I) Showed IC50 of 1 nM - 1 muM.

USE - For treating Alzheimer's disease (claimed); for treating diseases mediated by abnormal cleavage of amyloid precursor protein e.g. Cognitive impairment, Trisomy 21 (Down syndrome), cerebral amyloid angiopathy, degenerative dementia, hereditary cerebral hemorrhage with Amyloidosis of Dutch-Type, Creutzfeldt-Jakob disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stoke, pancreatitis, inclusion body myositis, other peripheral amyloidosis, diabetes and atherosclerosis.

ADVANTAGE - The compound inhibits the activity of beta-secretase or BACE thus preventing the formation of insoluble Abeta and arresting the production of Abeta.

CMC M2 *01* DCN: **RAH7RT-N RAH7RT-T**
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M2 *08* DCN: **RAH7RM-N RAH7RM-T**
M2 *09* DCN: **RAH7RL-N RAH7RL-T**
M2 *10* DCN: **RAH7RK-N RAH7RK-T**
M2 *11* DCN: **RAH7RJ-N RAH7RJ-T**
M2 *12* DCN: **RAH7RI-N RAH7RI-T**
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M2 *14* DCN: **RAH7RG-N RAH7RG-T**
M2 *15* DCN: **RAH7RF-N RAH7RF-T**
M2 *16* DCN: **RAH7RE-N RAH7RE-T**
M2 *17* DCN: **RAH7RD-N RAH7RD-T**
M2 *18* DCN: **RAH7RC-N RAH7RC-T**

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     M2 *22*    DCN: RAH7R8-N RAH7R8-T
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     M2 *25*    DCN: RAH7R5-N RAH7R5-T
     M2 *26*    DCN: RAH7R4-N RAH7R4-T
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     M2 *28*    DCN: RAH7R2-N RAH7R2-T
     M2 *29*    DCN: RAH7R0-N RAH7R0-T
     M2 *30*    DCN: RAH7QZ-N RAH7QZ-T
     M2 *31*    DCN: RAH7QY-N RAH7QY-T
     M2 *32*    DCN: RAH7QX-N RAH7QX-T
     M2 *33*

=> d his

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L1              STR

     FILE 'REGISTRY' ENTERED AT 08:49:07 ON 01 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 08:49:11 ON 01 MAY 2007
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L5            38 L4 AND NR>=3
L6               STR L1
L7             1 L6
L8            34 L6 FULL
                 SAV TEM J153C1/A L8
L9            34 L8 AND L4

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L15            0 L8

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                 EDIT /DSCE
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L18           1 E33-64
L19           1 L17/DCR
L20           1 L18-19
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FILE 'CASREACT' ENTERED AT 07:48:56 ON 02 MAY 2007
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FILE CONTENT:1840 - 29 Apr 2007 VOL 146 ISS 19

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identification.

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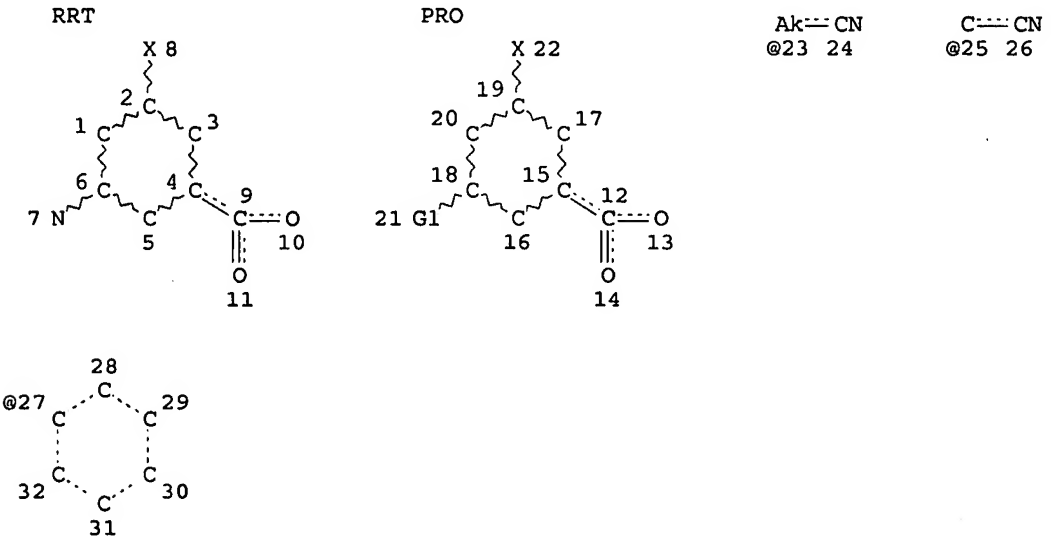


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STEREO ATTRIBUTES: NONE
L3            14 SEA FILE=CASREACT SSS FUL L1 (    22 REACTIONS)

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SEARCH TIME: 00.00.05

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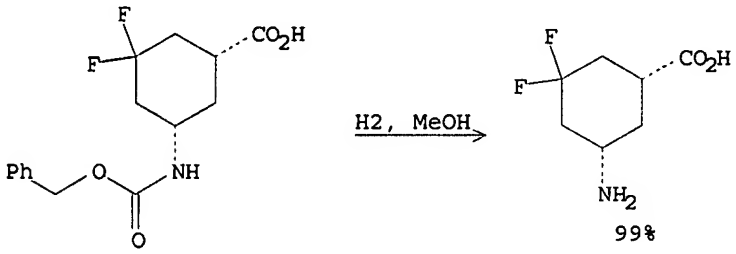
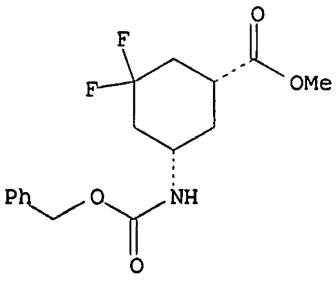
L3 ANSWER 1 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 144:381778 CASREACT
TI Syntheses and evaluation of fluorinated conformationally restricted analogues of GABA as potential inhibitors of GABA aminotransferase
AU Wang, Zhiyong; Silverman, Richard B.
CS Department of Chemistry, Department of Biochemistry, Molecular Biology, and Cell Biology, and the Center for Drug Discovery and Chemical Biology, Northwestern University, Evanston, IL, 60208-3113, USA
SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2242-2252
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier B.V.
DT Journal
LA English
AB Inhibition of γ-aminobutyric acid aminotransferase (GABA-AT) could raise the concentration of GABA, an inhibitory neurotransmitter in the human brain, and could have therapeutic applications for a variety of neurol. diseases including epilepsy. Four fluorine-containing analogs of GABA with conformations restricted by a cyclohexane ring system were designed and synthesized, but unlike some of their five-membered ring counterparts, minimal inhibition of GABA-AT was observed It is likely that the rigid chair conformation of these compds. cannot be accommodated well in the enzyme's active site.

RX(2) OF 78



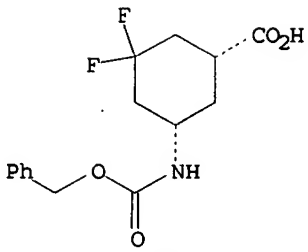
CON: overnight, room temperature

RX(14) OF 78



1. LiOH, Water, THF
2. HCl, Water

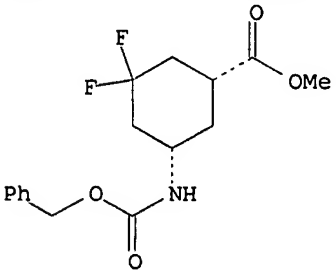
(step 1)



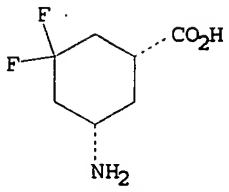
52%

CON: STAGE(1) overnight, room temperature
STAGE(2) room temperature, pH 1

RX(31) OF 78 - 2 STEPS



1.1. LiOH, Water, THF
1.2. HCl, Water
2. H2, MeOH



99%

CON: STEP(1.1) overnight, room temperature
STEP(1.2) room temperature, pH 1
STEP(2) overnight, room temperature

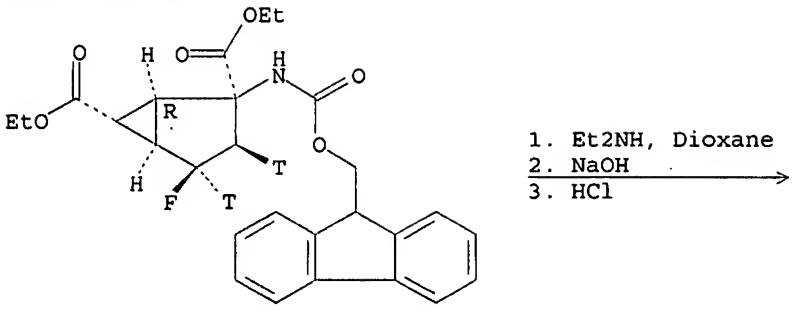
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File

Allan, R	1986	39	855	Aust J Chem	CAPLUS
Anet, F	1965	87	5250	J Am Chem Soc	CAPLUS
Aoyage, T	1990	38	1748	Chem Pharm Bull	
Becker, A	1983	39	4189	Tetrahedron	CAPLUS
Churchich, J	1981	256	1101	J Biol Chem	CAPLUS
Cooper, A	1985	113	80	Methods Enzymol	CAPLUS
Dess, D	1983	48	4155	J Org Chem	CAPLUS
Dewey, S	1998	30	119	Synapse	MEDLINE
Edmonds, M	2001	66	3747	J Org Chem	CAPLUS
Fernandez, M	2002	67	7587	J Org Chem	CAPLUS
Freidinger, R	1980	210	656	Science	CAPLUS
Fu, M	1999	7	1581	Bioorg Med Chem	CAPLUS
Gale, K	1989	30	1	Epilepsia	
Hornykiewicz, O	1976		479	GABA in Nervous Syst	CAPLUS
Jeffery, D	1988	28	347	Insect Biochem	
Katagiri, N	1997	38	1961	Tetrahedron Lett	CAPLUS
Krnjevic, K	1974	54	418	Physiol Rev	CAPLUS
Kushner, S	1999	290	797	J Pharmacol Exp Ther	CAPLUS
Middleton, W	1975	40	574	J Org Chem	CAPLUS
Murahashi, S	1989	54	3292	J Org Chem	CAPLUS
Nanavati, S	1989	32	2413	J Med Chem	CAPLUS
Neal, M	1977	138	169	Brain Res	CAPLUS
Olah, G	1979	44	1247	J Org Chem	CAPLUS
Osby, J	1984	25	2093	Tetrahedron Lett	CAPLUS
Perry, T	1973	288	337	New Eng J Med	MEDLINE
Qiu, J	1999	42	4725	J Med Chem	CAPLUS
Qiu, J	2000	43	706	J Med Chem	CAPLUS
Rando, R	1977	16	4604	Biochemistry	CAPLUS
Sasaki, T	1978	43	2320	J Org Chem	CAPLUS
Scott, E	1958	234	932	J Biol Chem	
Silverman, R	1981	20	1197	Biochemistry	CAPLUS
Silverman, R	1986	25	6817	Biochemistry	CAPLUS
Silverman, R	1980	45	815	J Org Chem	CAPLUS
Storici, P	1999	38	8628	Biochemistry	CAPLUS
Storici, P	2004	43	14057	Biochemistry	CAPLUS
Sugase, K	2004	47	489	J Med Chem	CAPLUS
Tian, F	2000	2	563	Org Lett	CAPLUS
Ye, Q	2002	67	9288	J Org Chem	CAPLUS

L3 ANSWER 2 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 143:97106 CASREACT
TI 1. Synthesis of LY455169-[2H2], a model study for the tritium labeling of LY459477. 2. Synthesis of LY459477-[3H2]
AU Kuo, Fengjiun; Kulanthaivel, Palaniappan; Rener, Gregory A.; Wheeler, William J.; Yi, Ping
CS Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 8th, Boston, MA, United States, June 1-5, 2003 (2004), Meeting Date 2003, 267-270. Editor(s): Dean, Dennis C.; Filer, Crist N.; McCarthy, Keith E. Publisher: John Wiley & Sons Ltd., Chichester, UK.
CODEN: 69FZAZ; ISBN: 0-470-86365-X
DT Conference
LA English
AB LY459477 is a potent mGluR agonist. Tritiated material was required for use in receptor binding assays. To support in vitro receptor binding studies, a tritium labeled isotopomer with a high specific activity (over 20 Ci/mmol) was required. The key to the tritiation of LY459477 was to find a method for the incorporation of tritium into protected LY455169. A general and simple method was developed for the synthesis of a double deuterium (or tritium) labeled alc. from the corresponding ketone. The preparation of LY459477-[3H] was accomplished by following the conditions developed in model studies.

RX(10) OF 28



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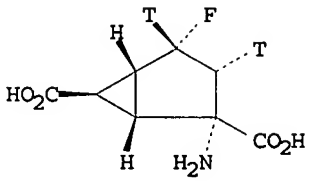

NOTE: no exptl. detail

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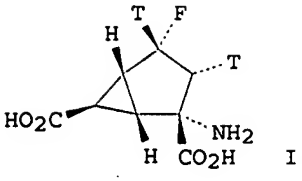
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Brown, H	1963		242	Hydroboration	
Djerassi, C	1948	70	417	J Am Chem Soc	CAPLUS
Fieser		1	1050	Reagents for Organic	
Fieser, L	1953	75	1700	J Am Chem Soc	CAPLUS
Goto, T	1961		513	Tetrahedron Lett	
Henbest, H	1955		2477	J Chem Soc	CAPLUS
Massey, S	1998		35	Eur Pat Appl, EP 878	
Sarma, J	1985		4657	Tetrahedron Lett	
Schenker, E	1961	73	81	Anger Chem	CAPLUS

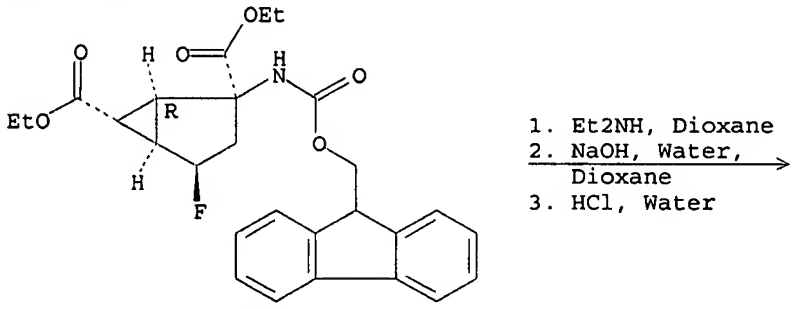
L3 ANSWER 3 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 142:240112 CASREACT
TI A method for the synthesis of 2-amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid-[3H2]
AU Kuo, Fengjiun; Kulanthaivel, Palaniappan; Rener, Gregory A.; Yi, Ping; Wheeler, William J.
CS Lilly Research Laboratories, A Division of Eli Lilly and Company Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Journal of Labelled Compounds & Radiopharmaceuticals (2004), 47(9), 571-581
CODEN: JLCRD4; ISSN: 0362-4803
PB John Wiley & Sons Ltd.
DT Journal
LA English
GI



I

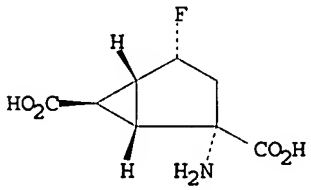
AB A process for double deuterium labeling of an alc. was developed. The process was utilized in the subsequent tritium labeling of a secondary alc. with high specific activity (24 Ci/mmol) by reduction of the corresponding ketone using sodium borotritide. The starting ketone was first brominated with pyridinium tribromide; the resulting alpha bromoketone was then reduced in THF/alc. in the presence of Ni(OAc)2. The alc. was then converted to dicarboxylic acid I, an mGluR agonist.

RX(7) OF 40



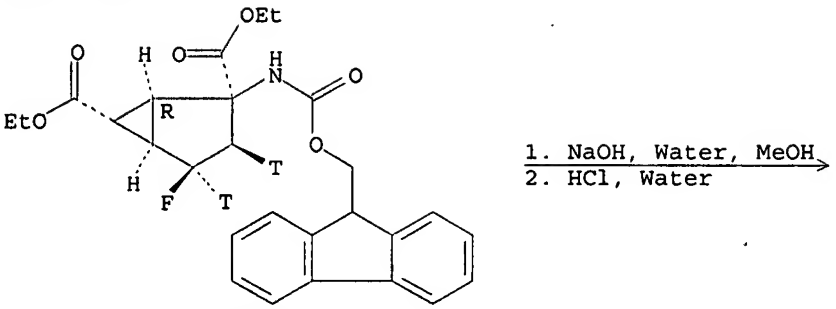
(step 1)

1. Et2NH, Dioxane
2. NaOH, Water, Dioxane
3. HCl, Water



CON: STAGE(1) overnight, room temperature
STAGE(2) overnight, room temperature
STAGE(3) room temperature

RX(10) OF 40



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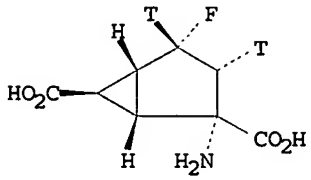
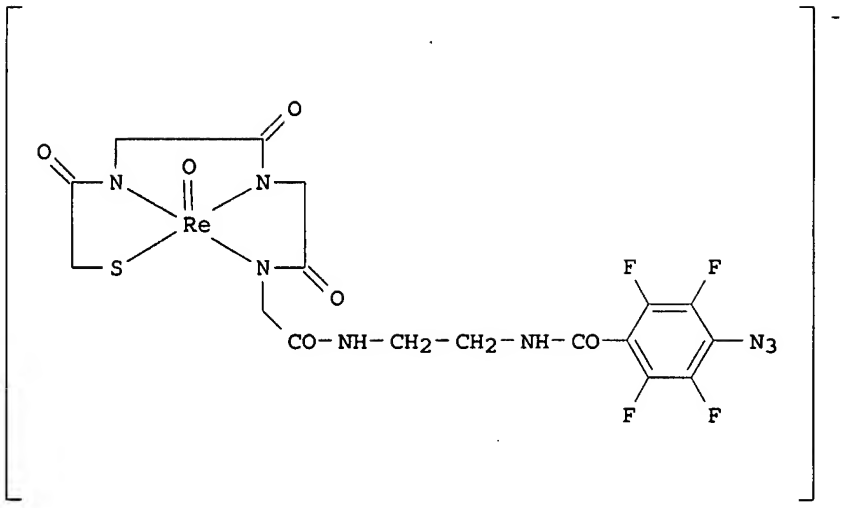


CON: STAGE(1) overnight, room temperature
STAGE(2) room temperature

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Brown, H	1963		242	Hydroboration	
Djerassi, C	1948	70	417	J Am Chem Soc	CAPLUS
Fieser, L	1953	75	1700	J Am Chem Soc	CAPLUS
Fieser and Fieser	1967	1	1050	Reagents for Organic	
Goto, T	1961	2	513	Tetrahedron Lett	
Henbest, H	1955		2477	J Chem Soc	CAPLUS
Massey, S	1998			EP-----0878463	CAPLUS
Mikami, K	1997	38	579	Tetrahedron Lett	CAPLUS
Sarma, J	1985	26	4657	Tetrahedron Lett	CAPLUS
Schenker, E	1961	73	81	Anger Chem	CAPLUS

L3 ANSWER 4 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 137:325389 CASREACT
TI Chemistry of Bifunctional Photoprobes. 6. Synthesis and Characterization of High Specific Activity Metalated Photochemical Probes: Development of Novel Rhenium Photoconjugates of Human Serum Albumin and Fab Fragments
AU Rajagopalan, Raghavan; Kuntz, Robert R.; Sharma, Uday; Volkert, Wynn A.; Pandurangi, Raghoottama S.
CS Department of Chemistry, University of Missouri, Columbia, MO, 65211, USA
SO Journal of Organic Chemistry (2002), 67(19), 6748-6757
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
GI



AB Functionalization of perfluoro aryl azides by bifunctional chelating agents (BFCAs) capable of forming high specific activity complexes with 99mTc (for γ-imaging) and 188Re (for radiotherapy) is described. The synthesis of multidonor BFCAs containing N2S2, N4, and N3S donor groups containing imidazole, pyridine, and pyrazine functionalities that may be important for tuning the pharmacokinetic parameters is also described. Functionalization of perfluoro aryl azides at various sites on BFCAs yields novel bifunctional photolabile chelating agents (BFPCAs) that are useful for covalent attachment to biomols. A representative Re-BFPCA I as the Me4N+ salt in a model solvent, diethylamine, proceeded to give a high yield of intermol. NH insertion product without the decomplexation of the metal ion from I. All products originated from the photolysis of I in diethylamine were characterized by anal. techniques, and a plausible mechanism of formation of different photolytic products is suggested. The high yield of intermol. NH insertion of I is extended to labeling of human serum albumin (HSA) and Fab fragments under aqueous conditions. The photolabeling technol. developed here offers a new way to attach diagnostically and therapeutically useful radiotracers (e.g., 99mTc, 188Re) to Fab fragments for potential noninvasive imaging and therapy of cancer.

RX(17) OF 59 - REACTION DIAGRAM NOT AVAILABLE
RETABLE

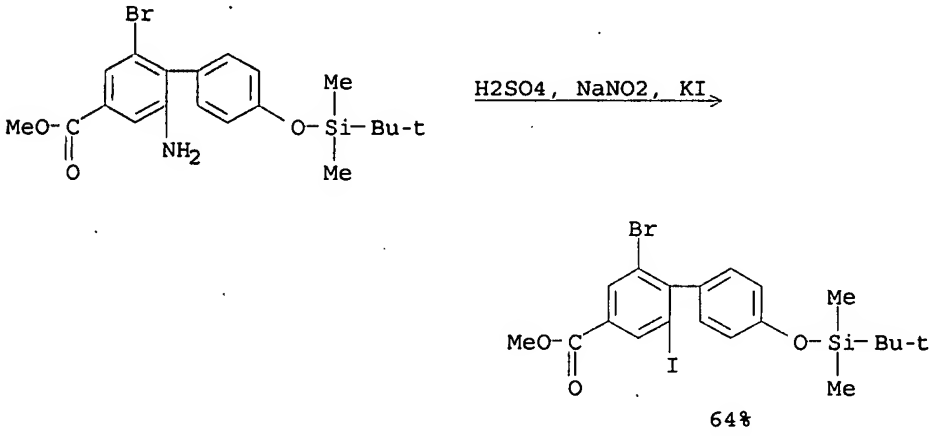
Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Alberto, R	1996	176	149	Top Curr Chem	CAPLUS
Amato, R	2000	126	161	Cancer Res Clin Onco	CAPLUS
Arano, Y	1999	59	128	Cancer Res	CAPLUS
Baldas, J	1999	41	1	Advances in Inorgani	
Barrera, J	1996	35	335	Inorg Chem	CAPLUS
Bell, R	1998	37	3517	Inorg Chem	CAPLUS
Bellar, G	1997	201	139	Adv Intern Med	
Bellar, G	2000	101	1465	Circulation	
Bellar, G	1991	535	451	Curr Probl Cardiol	
Bridger, G	1996	7	255	Bioconjugate Chem	CAPLUS
Bryson, N	1990	29	2948	Inorg Chem	CAPLUS
Cai, S	1992	57	1299	J Org Chem	CAPLUS
Canney, D	1993	36	1032	J Med Chem	CAPLUS
Cesati, R	2001	123	4093	J Am Chem Soc	CAPLUS
Das, T	2000	27	189	Nucl Med Biol	CAPLUS
Dilworth, J	1998	27	43	Chem Soc Rev	CAPLUS

Diwanji, M			5	Seminars in Nuclear	
Edwards, D	1999	99	2235	Chem Rev	
Ehrhardt, G	1991		159	Synthesis and Applic	
Fritzberg, A	1995		125	Chemical and Structu	CAPLUS
Fritzberg, A	1988	85	4025	Proc Natl Acad Sci U	CAPLUS
Fritzberg, A	1995		83	Targeted Delivery of	CAPLUS
Gene, M	1999	83	67	Pharmacol Therapeut	
Goldenberg, D	1980	40	2984	Cancer Res	MEDLINE
Goldenberg, D	1997	25	18	J Nucl Med Technol	CAPLUS
Goldenberg, D	1978	298	1384	N Engl J Med	MEDLINE
Goswami, N	1996	35	7546	Inorg Chem	CAPLUS
Griffiths, G	1992	3	91	Bioconjugate Chem	CAPLUS
Griffiths, G	1999	5	3001s	Clin Cancer Res	CAPLUS
Grummon, G	1995	34	1764	Inorg Chem	CAPLUS
Hansen, L	1992	31	280	Inorg Chem	
Hanson, L	1994	1	31	Metal-Based Drugs	
Herbert, J	1987			Nuclear Medicine The	
Hjelstuen, O	1995	120	863	Analyst	CAPLUS
Hom, R	1997	62	6290	J Org Chem	CAPLUS
Hom, R	1997	62	6290	J Org Chem	CAPLUS
Hom, R	1997	24	485	Nucl Med Biol	CAPLUS
Hunter, D	2000	11	175	Bioconjugate Chem	CAPLUS
Johannsen, B	1996	176	79	Top Curr Chem	
John, L	1997	41	111	J Nucl Med	
Jurisson, S	1993	93	1137	Chem Rev	CAPLUS
Kaplan, E	1978		237	Therapy in Nuclear M	
Karacay, H	2001	12	264	Bioconjugate Chem	
Kasina, S	1991	32	1445	J Nucl Med	CAPLUS
Katzenellenbogen, J	1997	17	1573	Anticancer Res	CAPLUS
Keana, J	1990	55	3640	J Org Chem	CAPLUS
Kniess, T	1999	240	657	J Radioanal Nucl Che	CAPLUS
Koppel, G	1990	1	13	Bioconjugate Chem	CAPLUS
Kowalsky, R			75	Chemistry of Radioph	
Law, K	1990	10	845	Anticancer Res	CAPLUS
Li, M	1994	5	101	Bioconjugate Chem	CAPLUS
Luyt, L	1999	10	470	Bioconjugate Chem	CAPLUS
Maddahi, J	1993	200	191	Nuclear Cardiology:S	
Mather, S	1994	38	481	J Nucl Biol Med	
Minutolo, F	1998	120	13264	J Am Chem Soc	CAPLUS
Noll, B	1992	43	899	Appl Radiat Isot	CAPLUS
O'Neil, J	1994	5	182	Bioconjugate Chem	CAPLUS
Pandurangi, R	1995	46	233	App Rad Isotopes	CAPLUS
Pandurangi, R	1995	6	630	Bioconjugate Chem	CAPLUS
Pandurangi, R	1997	25	77	Bioorg Chem	CAPLUS
Pandurangi, R	1996	35	3716	Inorg Chem	CAPLUS
Pandurangi, R	1998	120	11364	J Am Chem Soc	CAPLUS
Pandurangi, R	1995		565	J Chem Soc, Dalton T	CAPLUS
Pandurangi, R	1997	62	2587	J Org Chem	
Pandurangi, R	1998	63	9019	J Org Chem	CAPLUS
Pandurangi, R	2002			J Peptide Res, submi	
Pandurangi, R	1996	64	100	Photochem Photobiol	CAPLUS
Pandurangi, R	1997	65	101	Photochem Photobiol	
Pietzsch, H	2000	11	414	Bioconjugate Chem	CAPLUS
Poe, R	1993	4	172	Bioconjugate Chem	
Poe, R	1992	114	5054	J Am Chem Soc	CAPLUS
Polanc, S	1973	10	565	J Heterocycl Chem	CAPLUS
Polanc, S	1974	39	2143	J Org Chem	CAPLUS
Polanc, S	1976	41	3152	J Org Chem	CAPLUS
Polyakov, V	2000	11	762	Bioconjugate Chem	CAPLUS
Rajagopalan, R	1993			US-----5633372	CAPLUS
Rajagopalan, R	1997	8	407	Bioconjugate Chem	CAPLUS
Rao, T	1991	180	63	Inorg Chim Acta	CAPLUS
Rao, T	1990	112	5798	J Am Chem Soc	CAPLUS
Schmidt, P	1998	25	639	Nucl Med Biol	CAPLUS
Schubiger, P	1996	7	165	Bioconjugate Chem	CAPLUS
Scott, E	1997	8	146	Bioconjugate Chem	

Skaddan, M	1999	10	119	Bioconjugate Chem	CAPLUS
Skaddan, M	1999	64	8108	J Org Chem	CAPLUS
Skaddan, M	2000	27	269	Nucl Med Biol	CAPLUS
Spencer, R	1987			Radionuclides in The	
Spradau, T	1998	8	3235	Bioorg Med Chem Lett	CAPLUS
Srinivasan, A	1991			US-----5021556	CAPLUS
Sugiyura, Y	1978	17	2176	Inorg Chem	
Tsai, S	2001	12	264	Bioconjugate Chem	CAPLUS
Ultee, M	1997	38	133	J Nucl Med	CAPLUS
Vangog, F	1996	37	352	J Nucl Med	CAPLUS
Volkert, W	1999	99	2269	Chem Rev	CAPLUS
Volkert, W	1996		123	Topics in Current Ch	CAPLUS
Wilber, D	1992	3	433	Bioconjugate Chem	
Wust, F	1999	7	1827	Bioorg Med Chem	CAPLUS
Wust, F	1998	63	665	Steroids	CAPLUS
Yamamura, N	1999	10	489	Bioconjugate Chem	CAPLUS

L3 ANSWER 5 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 135:257002 CASREACT
TI Biphenyls as surrogates of the steroidal backbone. Part 1. Synthesis and estrogen receptor affinity of an original series of polysubstituted biphenyls
AU Lesuisse, D.; Albert, E.; Bouchoux, F.; Cerede, E.; Lefrancois, J.-M.; Levif, M.-O.; Tessier, S.; Tric, B.; Teutsch, G.
CS Medicinal Chemistry, Aventis, Romainville, 93235, Fr.
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(13), 1709-1712
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Substituted biphenyls were prepared and evaluated for their binding affinity for the estrogen receptor. Some of them demonstrated binding better than or equivalent to that of estradiol.

RX(24) OF 53



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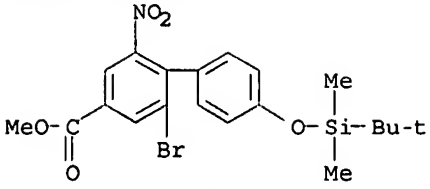
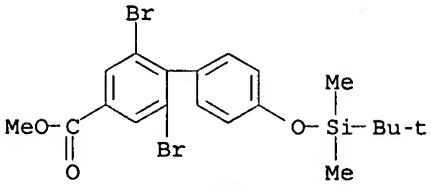
RX(27) OF 53



(step 1)

1. Pd(OH)2, Cyclohexene
2. R:594-70-7, CHBr3, CHCl3



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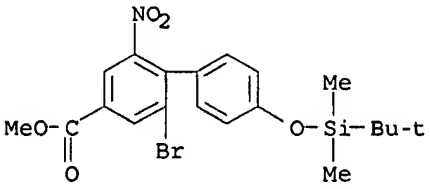
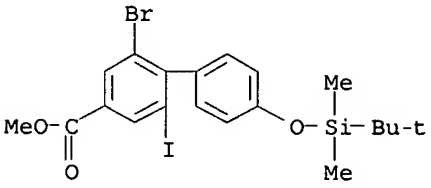
RX(35) OF 53 - 2 STEPS



1. Pd(OH)2, Cyclohexene
2. H2SO4, NaNO2, KI



64%

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anstead, G	1989	32	2163	J Med Chem	CAPLUS
Anstead, G	1990	33	2726	J Med Chem	CAPLUS
Beck, J	1987	24	267	J Heterocycl Chem	CAPLUS
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Bindal, R	1990	112	7861	J Am Chem Soc	CAPLUS
Chae, K	1991	40	806	Mol Pharmacol	CAPLUS
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Erdik, E	1992	48	9577	Tetrahedron	CAPLUS
Fanta, P	1974	1	9	Synthesis	
Field, L	1977	99	5249	J Am Chem Soc	CAPLUS
Frazer, M	1989	25	255	In Vitro Cell Dev Bi	
Grega, K	1995	60	55	J Org Chem, Book of	
Griffin, M	1990	16	269	Endocr Res	CAPLUS
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Hagmeyer, K	1999	15	37	J Pharm Technol	CAPLUS
Huth, A	1989	45	6679	Tetrahedron	CAPLUS
Jordan, V	1984	36	245	Pharmacol Rev	CAPLUS

Korach, K	1979	254	8963	J Biol Chem	CAPLUS
Korach, K	1988	33	120	Mol Pharmacol	CAPLUS
Korach, K	1978	75	468	Proc Natl Acad Sci U	CAPLUS
Korach, K	1991	56	263	Steroids	CAPLUS
Kress, T	1988	10	803	Synthesis	
Krishnan, A	1993	132	2279	Endocrinology	CAPLUS
Kumada, M	1990	21	845	Tetrahedron Lett	
Mitchell, M	1991	32	2273	Tetrahedron Lett	CAPLUS
Miyaura, N	1995	95	2457	Chem Rev	CAPLUS
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Negishi, E	1982	15	340	Acc Chem Res	CAPLUS
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Nique, F	1999	50	21	J Steroid Biochem Mo	
Oh-E, T	1990	4	221	Synlett	
Rhee, C	1995	5	133	Bioorg Med Chem Lett	CAPLUS
Stauffer, S	2000	43	4934	J Med Chem	CAPLUS
Sun, J	1999	1403	800	Endocrinology	
Swindell, C	1990	31	5405	Tetrahedron Lett	CAPLUS
Swindell, C	1990	31	5405	Tetrahedron Lett	CAPLUS
Tilley, J	1989	32	1814	J Med Chem	CAPLUS
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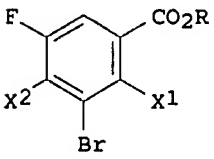
Von Angerer, E	1990	33	2635	J Med Chem	CAPLUS
Watanabe, T	1992	3	207	Synlett	

L3 ANSWER 6 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 132:78365 CASREACT
TI Preparation of 3-bromo-5-fluorobenzoic acid derivatives
IN Kurumaya, Mitsuo; Honda, Tsunetoshi
PA Tohkem Products Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP2000016971	A	20000118	1998JP-0180465	19980626
PRAI 1998JP-0180465	19980626			

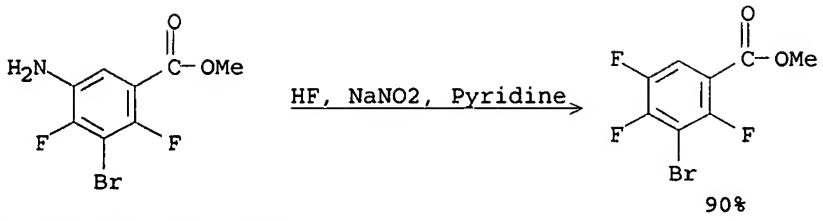
OS MARPAT 132:78365
GI



I

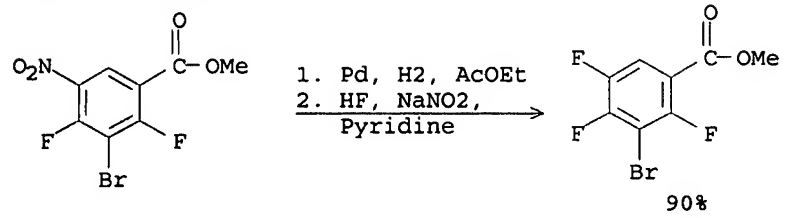
AB Title compds. I (R = H, alkyl; X1, X2 = halo) are prepared by bromination of 2,4-dihalo-5-nitrobenzoic acid derivs. followed by reduction, diazotization, and fluorination. Thus, bromination of Me 2,4-difluoro-5-nitrobenzoate with potassium bromate in 85% H2SO4 gave 68% Me 3-bromo-2,4-difluoro-5-nitrobenzoate, reduction of which with H2 in EtOAc in the presence of 5% Pd/C gave 70% Me 3-bromo-2,4-difluoro-5-aminobenzoate. Diazotization of the latter compound followed by fluorination gave 90% Me 3-bromo-2,4,5-triflurobenzoate.

RX(3) OF 6



NOTE: 2nd step photochem.

RX(5) OF 6 - 2 STEPS

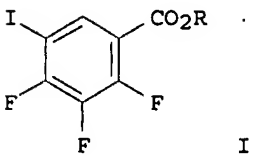


NOTE: 2) 2nd step photochem.

L3 ANSWER 7 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 130:237364 CASREACT
TI Preparation of 2,3,4-trifluoro-5-iodobenzoic acid and its esters
IN Yoneda, Yasuhiro; Yokota, Naoyuki; Ataka, Kikuo
PA Ube Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

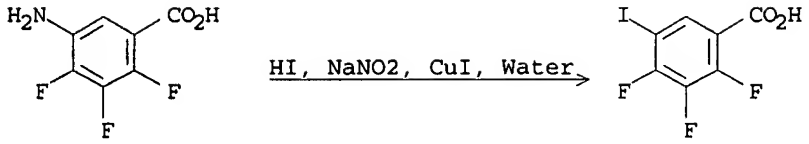
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP--11080076	A	19990323	1997JP-0338495	19971209
	JP---3573249	B2	20041006		

PRAI 1997JP-0182766 19970708
OS MARPAT 130:237364
GI



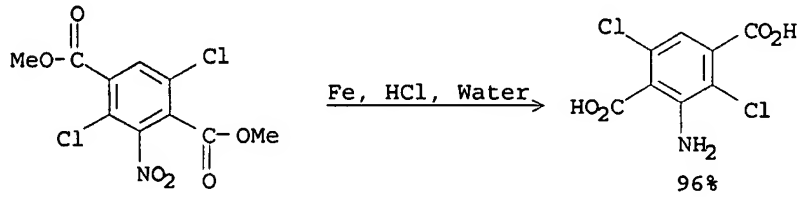
AB Title compds. I (R = H, C1-10 alkyl, C3-10 cycloalkyl, C7-10 aralkyl) were prepared by reaction of 5-amino-2,3,4-trifluorobenzoic acid (II) with HI, alkali metal nitrites, and CuX (X = halo) in solvents. Thus, reaction of II with aqueous HI, CuI, and NaNO2 in H2O gave 2,3,4-trifluoro-5-iodobenzoic acid, refluxing of which with EtOH in toluene in the presence of H2SO4 gave Et 2,3,4-trifluoro-5-iodobenzoate.

RX(1) OF 1



L3 ANSWER 8 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 117:69511 CASREACT
TI Preparation of 2,5-dichloro-3-aminobenzoic acid
AU Yazlovitskii, A. V.; Ral'chuk, I. A.; Shcherbina, F. F.; Grigor'ev, A. A.
CS Inst. Bioorg. Khim. Neftekhim., Kiev, Ukraine
SO Zhurnal Prikladnoi Khimii (Sankt-Peterburg, Russian Federation) (1991), 64(10), 2201-2
CODEN: ZPKHAB; ISSN: 0044-4618
DT Journal
LA Russian
AB Refluxing 2,5,3,6-Cl2(MeO2C)2C6HNO2 with Fe shavings and concentrated HCl in Et2O gave 96% 2,5,3,6-Cl2(HO2C)2C6HNH2, which was decarboxylated by addnl. reflux in 1:1 H2O-concentrated HCl to give 95% title compound

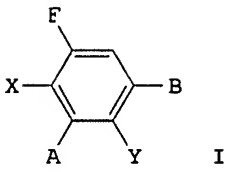
RX(1) OF 3



L3 ANSWER 9 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 116:193920 CASREACT
TI Preparation of fluorobenzoic acids as antibacterial intermediates
IN Kumai, Seisaku; Seki, Takashi; Wada, Akihiro
PA Asahi Glass Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP--03275647	A	19911206	1990JP-0075534	19900327
PRAI 1990JP-0075534	19900327			

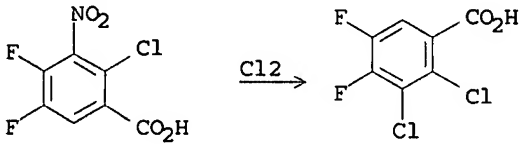
OS MARPAT 116:193920
GI



I

AB The title compds. I (A = Y = Cl, B = CO2H, X = F or Cl), useful as antibacterial intermediates, are prepared by Friedel-Crafts acylation of I (A = B = H, Y = Cl), haloform reaction of I (A = H, B = Ac, Y = Cl), nitration of I (A = H, B = CO2H, Y = Cl), and chlorination of I (A = NO2, B = CO2H, Y = Cl) with chlorinating agents. The title compds. I (A = Cl, B = CO2H, X = F, Y = F or Cl) are prepared by chlorination of I (A = X = Y = Cl, B = CO2H), fluorination of I (A = X = Y = Cl, B = COCl), and hydrolysis of I (A = Cl, B = COF, X = F, Y = F, Cl). Friedel-Crafts acylation of 3,4-difluorochlorobenzene with AcCl and AlCl3 gave 74% I (A = H, B = Ac, X = F, Y = Cl) which was subjected to a haloform reaction to give 85.3% I (A = H, B = CO2H, X = F, Y = Cl) (II). Nitration of II by H2SO4-HNO3 mixture gave 54% I (A = NO2, B = CO2H, X = F, Y = Cl) which was chlorinated by Cl to give 80% I (A = Y = Cl, B = CO2H, X = F).

RX(4) OF 10

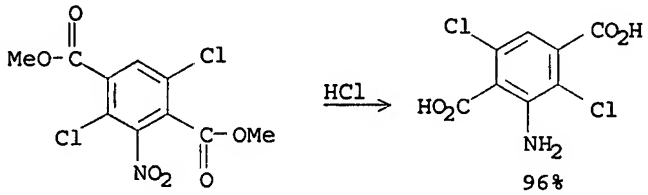


L3 ANSWER 10 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 113:97198 CASREACT
TI Preparation of 2,5-dichloro-3-aminobenzoic acid
IN Ral'chuk, I. A.; Yazlovitskii, A. V.; Shcherbina, F. F.; Grigor'ev, A. A.
PA Institute of Physical-Organic Chemistry and Coal Chemistry, Kiev, USSR
SO U.S.S.R.
From: Otkrytiya, Izobret. 1990, (10), 104.
CODEN: URXXAF
DT Patent
LA Russian
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU---1549947	A1	19900315	1988SU-4427546	19880519

PRAI 1988SU-4427546 19880519
AB The title compound was prepared by reduction of di-Me 2,5-dichloro-3-nitroterephthalate by Fe in HCl followed by decarboxylation of the diacid.

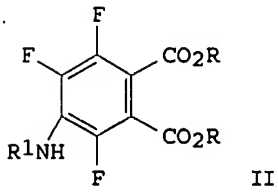
RX(2) OF 3



L3 ANSWER 11 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 112:216450 CASREACT
TI Synthesis of 3-chloro-2,4,5-trifluorobenzoic acid as intermediate for antibacterial agents
IN Wemple, James N.; Karrick, Gregory L.; Spence, Floyd G.
PA Warner-Lambert Co., USA
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US---4885386	A	19891205	1988US-0264296	19881028
CA---1313883	C	19930223	1989CA-0613205	19890926
DK---8905377	A	19900429	1989DK-0005377	19891027
EP----366149	A1	19900502	1989EP-0120030	19891027
EP----366149	B1	19930113		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP--02178254	A	19900711	1989JP-0278761	19891027
JP---2886908	B2	19990426		
AT-----84518	T	19930115	1989AT-0120030	19891027
ES---2053908	T3	19940801	1989ES-0120030	19891027

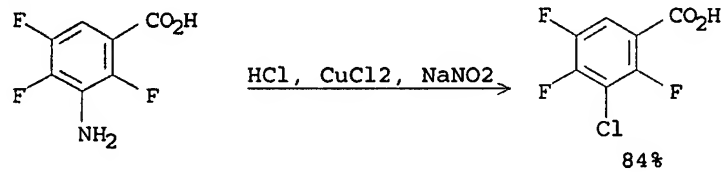
PRAI 1988US-0264296 19881028
1989EP-0120030 19891027
OS MARPAT 112:216450
GI



II

AB The title compound (I), useful as intermediate for quinolone antibacterial agents, was prepared from benzenedicarboxylates II (R = alkyl; R1 = tert-Bu, PhCH2, etc.). A mixture of 4-[(1,1-dimethylpropyl)amino]-3,5,6-trifluoro-1,2-benzenedicarboxylic acid di-Me ester and 36% aqueous HCl was refluxed for 20 h to give 3-amino-2,4,5-trifluorobenzoic acid, which was treated with NaNO2 and CuCl2 in aqueous HCl to give I.

RX(1) OF 2



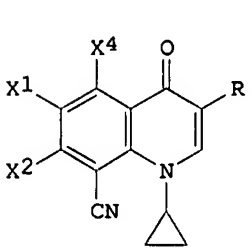
84%

L3 ANSWER 12 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 109:230824 CASREACT
TI 8-Cyano-1-cyclopropylquinolonecarboxylic acids as antibacterial agents
IN Schriewer, Michael; Grohe, Klaus; Petersen, Uwe; Haller, Ingo; Metzger, Karl Georg; Endermann, Rainer; Zeiler, Hans Joachim

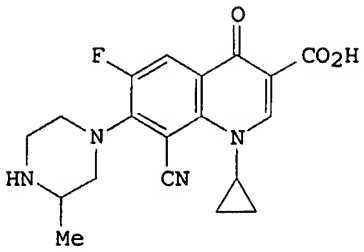
PA Bayer A.-G., Fed. Rep. Ger.
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE---3702393	A1	19880811	1987DE-3702393	19870128
US---4908366	A	19900313	1988US-0144884	19880114
EP----276700	A1	19880803	1988EP-0100503	19880115
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
CA---1314544	C	19930316	1988CA-0557311	19880126
JP--63201170	A	19880819	1988JP-0014771	19880127
US---5051418	A	19910924	1989US-0434666	19891113
US---5190955	A	19930302	1991US-0645751	19910125
PRAI 1987DE-3702393	19870128			
1988US-0144884	19880114			
1989US-0434666	19891113			

OS MARPAT 109:230824
GI



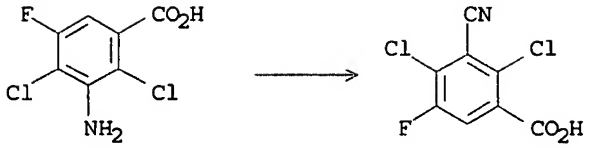
I



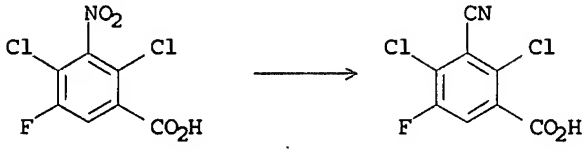
III

AB The title compds. [I; R = CO2H, cyano, CO2R1, CONR2R3; R1 = alkyl; R2 = H, alkyl; R3 = R2, (un)substituted Ph; X1 = H, NO2, alkyl, halo; X2 = heterocyclyl; X4 = H, halo, alkyl] were prepared as antibacterial agents (no data). 2,4,5,3-Cl2F(NC)C6HCOCH2CO2Et (preparation given) was heated 2 h at 150° with HC(OEt)3 in Ac2O to give 2,4,5,3-Cl2F(NC)C6HCOC(:CHR4)CO2Et (II; R4 = OEt) which was stirred 2 h with cyclopropylamine in EtOH to give II (R = cyclopropylamino). The latter was stirred 24 h in dioxane containing KOCMe3 to give, after saponification, I (R = CO2H, X1 = F, X2 = Cl, X4 = H) which was heated 3 h in dioxane with 2-methylpiperazine to give title compound III. Tablets were prepared each containing III 583.0, cellulose 55.0, starch 72.0, polyvinylpyrrolidone 30.0, silica 5.0, and Mg stearate 5.0 mg coated with poly(O-hydroxypropyl-O-methyl)cellulose 6.0, Macrogol 4000 2.0, TiO2 2.0 mg, and polyethyleneglycol (no amount given).

RX(3) OF 15



RX(7) OF 15 - 2 STEPS



L3 ANSWER 13 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 109:73145 CASREACT
TI Process for preparing benzoic acid derivatives useful as antibacterial intermediates
IN Petersen, Uwe; Schriewer, Michael; Kysela, Ernst; Grohe, Klaus
PA Bayer A.-G., Fed. Rep. Ger.
SO Ger. Offen., 11 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE---3631906	A1	19880331	1986DE-3631906	19860919
	US---4851160	A	19890725	1987US-0090888	19870828
	NO---8703689	A	19880321	1987NO-0003689	19870903
	NO----166785	B	19910527		
	NO----166785	C	19910904		
	EP----266512	A2	19880511	1987EP-0113034	19870907
	EP----266512	A3	19890503		
	EP----266512	B1	19911204		
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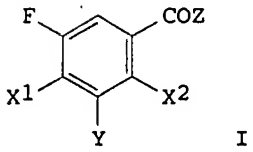
	AT-----70045	T	19911215	1987AT-0113034	19870907
	ES---2044886	T3	19940116	1987ES-0113034	19870907
	AU---8778290	A	19880324	1987AU-0078290	19870911
	AU----600020	B2	19900802		
	IL-----83919	A	19910630	1987IL-0083919	19870916
	FI---8704063	A	19880320	1987FI-0004063	19870917
	FI-----86843	B	19920715		
	FI-----86843	C	19921026		
	DD----269146	A5	19890621	1987DD-0307030	19870917
	CA---1325018	C	19931207	1987CA-0547091	19870917
	DK---8704902	A	19880320	1987DK-0004902	19870918
	DK----168212	B1	19940228		
	JP--63088157	A	19880419	1987JP-0232702	19870918
	JP--05076934	B	19931025		
	ZA---8707027	A	19880525	1987ZA-0007027	19870918
	HU-----45001	A2	19880530	1987HU-0004174	19870918
	HU----197872	B	19890628		
	CN--87106482	A	19880330	1987CN-0106482	19870919
	CN---1024415	B	19940504		
	US---4990661	A	19910205	1989US-0330396	19890329
	JP--06025125	A	19940201	1993JP-0124640	19930430
	JP--06094446	B	19941124		
	DK---9300861	A	19930721	1993DK-0000861	19930721
	DK----170253	B1	19950717		

PRAI 1986DE-3631906 19860919

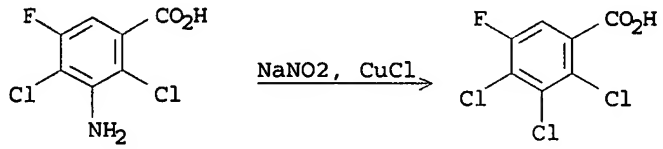
1987US-0090888 19870828
1987EP-0113034 19870907
OS MARPAT 109:73145
GI



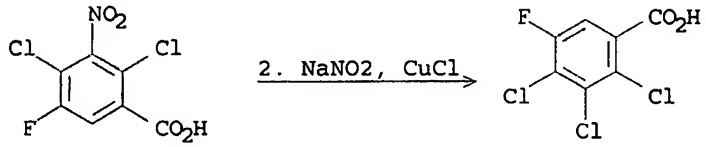
I

AB Title compds. I (X1, X2 = F, Cl; Y = F, Cl, Br, iodo; Z = F, Cl, OH), useful as antibacterial intermediates, are prepared Diazotization of 3-amino-2,4-dichloro-5-fluorobenzoic acid and treatment with CuCl gave 94% I (Z = OH, X1, X2, Y = Cl).

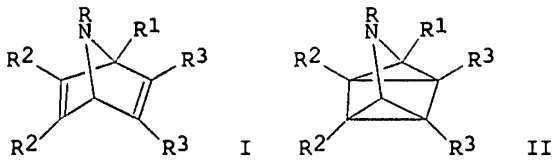
RX(4) OF 21



RX(8) OF 21 - 2 STEPS



L3 ANSWER 14 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
AN 105:24171 CASREACT
TI Photochemical transformations. 65. The 3σ → 3π-route to 1H-azepines/benzene imines
AU Prinzbach, Horst; Bingmann, Horst; Fritz, Hans; Markert, Juergen; Knothe, Lothar; Eberbach, Wolfgang; Brokatzky-Geiger, Juergen; Sekutowski, Janine C.; Krueger, Carl
CS Chem. Lab., Univ. Freiburg, Freiburg/Br., D-7800, Fed. Rep. Ger.
SO Chemische Berichte (1986), 119(2), 616-44
CODEN: CHBEAM; ISSN: 0009-2940
DT Journal
LA German
GI



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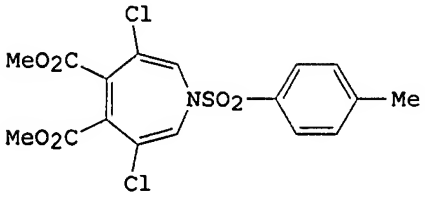
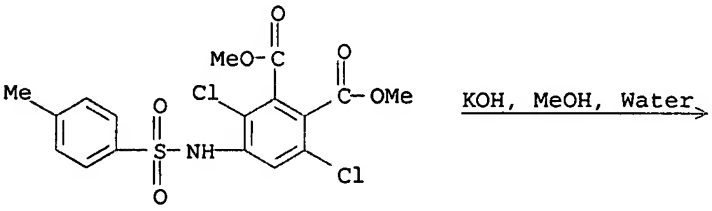
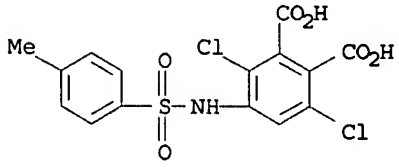


III

AB With several newly prepared substrates the influence of substituents upon the individual steps in the 3σ→3π-route to 1H-azepines is more precisely defined. The 7-azanorbornadienes I (R = tosyl, CO2CH2CH:CH2; R1 = H, CH2OCH2C.tplbond.CH; R2 = H, Cl; R3 = H, CO2Me) are selectively isomerized by sensitized or direct photoexcitation into the azaquadricyclanes II, some of which are highly unstable. For the thermal conversion of II (R = tosyl, R1 = R3 = H) the kinetic parameters have been determined (benzene); Ea = 28.0 ± 0.2 kcal/mol, lg A = 15.7; ΔH.thermod. = 27.3 ± 0.2 kcal/mol, ΔS.thermod. = 1.1 ± 0.7 e.u. This barrier is lowered more efficiently in II (R2 = Cl) than in II (R3 = CO2Me) with the former and latter causing exclusive scission of the opposite and neighboring cyclopropane bonds resp. The intermediate azomethine ylides are captured with dipolarog. reagents more or less efficiently depending on their substitution pattern. In II (R = tosyl, R1 = CH2OCH2C.tplbond.CH, R2 = H, R3 = CO2Me) the intramol. addition of the unactivated yne component at -30° is so fast, that azepine formation is almost totally suppressed. The azepinebenzeneimine equilibrium mixture from II (R = tosyl, R1 = H, R2 = Cl, R3 = CO2Me) (.apprx.9:1) crystallizes as the azepine III (x-ray crystal structure anal.).

RX(30) OF 135





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